

ABSTRACT

The invention includes methods for reducing alcohol consumption in mammals by inhibiting expression of an aldehyde dehydrogenase (e.g., liver mitochondrial aldehyde dehydrogenase) in cells of the mammal. Expression of the aldehyde dehydrogenase can be inhibited by administering (locally or systemically) an antisense oligonucleotide (e.g., one 12-2000 residues in length) to the mammal, whereby expression of a relatively active allele of an aldehyde dehydrogenase gene can be inhibited. Aldehyde dehydrogenase activity can also be inhibited in the cells of a mammal, for the same purposes, by administering to the cells an expression vector encoding an inactive allele dominant of the aldehyde dehydrogenase. Upon expression, subunits of the protein encoded by the inactive allele can coalesce with one another or with subunits of the cells normally-expressed aldehyde dehydrogenase to lower the level of aldehyde dehydrogenase activity in the cell. The invention also relates to methods for predicting whether an antisense oligonucleotide (ASO) will be efficacious for inhibiting expression of a gene.